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Abstract: Following the collapse of the Soviet Union in 1991, there was an increase in the number of cases of human echinococcosis recorded throughout central Asia. Between 1991 and 2001 incidence rates of cystic echinococcosis (CE) increased by 4 fold or more. There also appeared to be increases in prevalence of CE in livestock and prevalences of Echinococcus granulosus reported in dogs. The increase in human echinococcosis was associated with changes in livestock husbandry, decline in veterinary public health services, increases in dog populations and increased poverty, all of which served to promote transmission of E. granulosus. A few years after reports of increased transmission of E. granulosus, the first reports of E. multilocularis infection in dogs were recorded. Further studies indicated that in both Kazakhstan and Kyrgyzstan prevalences of up to 18% were present. Recently there has been a dramatic increase in the number of cases of human alveolar echinococcosis recorded in Kyrgyzstan with over 60 cases reported in 2011.

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The emergence of echinococcosis in central Asia

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SUMMARY

Following the collapse of the Soviet Union in 1991, there was an increase in the numbers of cases of human echinococcosis recorded throughout central Asia. Between 1991 and 2001 incidence rates of cystic echinococcosis (CE) increased by 4 fold or more. There also appeared to be increases in prevalence of CE in livestock and prevalences of *Echinococcus granulosus* reported in dogs. The increase in human echinococcosis was associated with changes in livestock husbandry, decline in veterinary public health services, increases in dog populations and increased poverty all of which served to promote transmission of *E. granulosus*. A few years after reports of increased transmission of *E. granulosus*, the first reports of *E. multilocularis* infection in dogs were recorded. Further studies indicated that in both Kazakhstan and Kyrgyzstan prevalences of up to 18% were present. Recently there has been a dramatic increase in the number of cases of human alveolar echinococcosis recorded in Kyrgyzstan with over 60 cases reported in 2011.

Key words: Emergence, cystic echinococcosis, alveolar echinococcosis, *Echinococcus granulosus*, *Echinococcus multilocularis*, epidemiology.

Running title: Echinococcosis in Central Asia

INTRODUCTION

The collapse of the Soviet Union in 1991 was followed by severe economic hardship and was associated with increases in mortality and decreases in life expectancy across the region (Becker and Hemley, *1998*; Becker and Urzhumova, *2005*; Stillman, *2006)*. At the end of last decade of the 20th century it became apparent that there was evidence of increased numbers of human cystic echinococcosis (CE) in the former Soviet Republics of central Asia (Table 1). Official government statistics in Kazakhstan document an increase in cases of CE from about 200 cases per year until 1994, rising rapidly to approximately 1000 cases per year by the beginning of the 21st century (Torgerson *et al. 2002*). This epidemic emerged at a time of rapid economic decline, and decreases in medical services and hence was unlikely to be an artefact caused by improved diagnosis. Likewise there was strong evidence from neighbouring Kyrgyzstan that a similar phenomenon was present (Torgerson *et al. 2003b*). In Tajikistan it was reported that the number of cases increased from 374 cases in 1992 to 1875 cases in 2002 (Muminov *et al. 2004*). Subsequently data became available that confirmed there similar epidemics were occurring in Uzbekistan and Turkmenistan (Torgerson *et al. 2006*). Furthermore in Uzbekistan there is very strong evidence that officially reported cases are a substantial underestimate of the numbers of cases being treated. A detailed case finding study of all hospitals in Uzbekistan uncovered approximately four times the numbers of cases of CE then were being reported in Government statistics (Nazirov *et al. 2002*). Unpublished figures suggest that the numbers of cases of CE, at least in Kazakhstan and Kyrgyzstan have stabalised since about 2003. However, there are now increasing numbers of human cases of alveolar echinoccocsis (AE) being reported in Kyrygzstan (Usubalieva *et al. 2013*).

EPIDEMIOLOGY OF *ECHINOCOCCUS GRANULOSUS*

Human studies.

Information regarding the epidemiology of the disease in humans has been obtained from hospital records, official data of reported cases or from a limited number of ultrasound surveillance community studies. Official data and hospital records indicates that there are many cases in children under 14 years of age – possibly up to one third (Torgerson *et al. 2002, 2003a*). However, although the mean age of cases from a detailed hospital survey in Kyrgyzstan is very young – approximately 24 years (Torgerson *et al. 2003a*) this is not dissimilar to the median age of the population (see data in US Census Bureau, *2012*) and the proportion of the Kyrgyz population under 14 years is approximately 35%. Thus, at least in Kyrgyzstan, an important factor is the very young age pyramid of the population. However in the hospital study, the proportion of paediatric cases was somewhat higher after 1997 compared to prior to 1997. This indicates an increasing proportion of children and is consistent with the origins of the epidemic being recent. Other than the young age of cases, there is also an association with unemployment amongst adults – the proportion of adults diagnosed with CE who were unemployed was double that of the general unemployment rate in the country. A further interesting observation was that those individuals with hepatic cysts tended to be younger than those with pulmonary cysts.

In Kazakhstan the origin of human cases is closely associated with the major sheep rearing areas of the country (Torgerson *et al. 2002*). In Tajikistan there seem to be a lower proportion of paediatric cases with 7.8% of cases being less than 14 years of age and 58.7% being between 18 and 48 years and the average age of hospital treated patients being 36 years of age (Muminov *et al. 2004*). Most cases (89%) originated from rural areas. Women were over represented (60.3%). In addition the incidence varies in different regions. The northern part of the country has the highest incidence being more than twice that of central areas. The southern districts seem to be intermediate in incidence. In Uzbekistan approximately 14.3% of cases treated between 1999 and 2001 were in children less than 14 years of age, although the proportion of paediatric cases was increasing. Of the adults, 54% of cases were in women, 46% men (Nazirov *et al. 2002*).

Community studies using ultrasound surveillance have also given further clues to the epidemiology of CE in this region. In Kyrgyzstan a cross-sectional ultrasound survey of 1,486 subjects in the Kochkor district revealed 20 with abdominal cysts. This gives an estimated prevalence of 1.35%. However, because of bias in the population surveyed and potential missing data, the true prevalence of CE might be as high as 3.4% (Torgerson *et al. 2003a*). Both these estimates were significantly higher than a survey undertaken in the same area some 10 years previously. Logistic regression revealed that there was an association with infection and the provision of a poor water supply. In a rural community in the east of Kazakhstan 47 cases, either ultrasound positive or recently treated, out of a population of 3,126 were revealed to have CE (Torgerson *et al. 2009a*). The estimated incidence in this population was 50 cases per 100,000 per year between 2000 and 2005. Large households and /or poor living standards were significantly associated with a diagnosis of CE. Subjects diagnosed with CE also were unable to work for longer periods of time.

There is also one study that demonstrated that there is widespread environmental contamination of the surroundings of rural homes with *E. granulosus* eggs (Shaikenov *et al. 2004*) . Five of 120 soil samples taken from 30 gardens of rural homesteads were positive for the G1 strain of *E. granulosus* demonstrating the potential for indirect transmission of *E. granulosus* to humans from such sources.

Livestock studies

There have been several studies investigating the increasing prevalence of CE in livestock which has paralleled the increase in human disease incidence. In Uzbekistan the prevalence of echinococcosis in sheep for example has increased from 45% to 62 % between 1990 and 2002 (Aminjanov and Aminjanov, *2004*). In Kazakhstan prevalences in sheep have also increased. In the 1980s prevalences of approximately 14% were reported in southern Kazakhstan. By 2000 this had increased to 37% in the same area (Torgerson *et al. 2002*). In the Naryn region of central Kyrgyzstan a prevalence of 64% in sheep was reported in 2006 (Torgerson *et al. 2009b*). In Tajikistan prevalence varies with region. In high endemic areas in the north, over 50% of sheep are infected, in central and southern districts sheep generally have approximately a 20% prevalence and areas around the Chinese border just 7%. Infection varies with age in all regions with young animals having often less than a 10% prevalence, but the oldest animals having prevalences approaching 80% (Muminov *et al. 2004*). There is also some limited data on prevalences in pigs, camels and goats in Uzbekistan and Tadjikistan (see Table 2).

There is also information regarding the transmission dynamics in livestock. In southern districts of Kazakhstan the prevalence in sheep has been reported at between 34 and 48% and cattle at approximately 7% (Torgerson *et al. 2003b*). In sheep there was a mean abundance of 2.54 cysts per sheep from South Kazakhstan and Jambyl Oblasts rising to 4.7 cysts per sheep for other regions. There is increasing abundance and prevalence with age in both populations with sheep acquiring 1.2 and 2.0 cysts per year. Cattle had a much lower infection pressure only acquiring 0.15 cysts per year. The reasons for apparent lower infection pressure in cattle compared to sheep is not known, but it could be due to variation in infection pressure through different grazing patterns, variations in parasite genotype between the two species, or the genotype circulating being less infectious to cattle compared to sheep. In the Naryn district of Kyrgyzstan the infection pressure in sheep has been estimated at 1.3 cysts per year – comparable to that seen in neighbouring Kazakhstan (Torgerson *et al. 2009b*). More detailed analysis was undertaking of the data from Kyrgyzstan with an analysis of the infectious biomass in sheep in terms of the number of infectious protoscoleces. It was demonstrated that 80% of the infective biomass was in sheep aged 4 years or older, but this represented just 28% of sheep presented for slaughter.

*Studies in definitive host*s

Dogs play an essential role in the transmission cycle of *E. granulosus* and transmission to man. There have been a number of studies investigating the prevalence and transmission dynamics of *E. granulosus* in dogs across this region. In Tajikistan one study of 120 dogs reported a prevalence of 15.2% (Muminov *et al. 2004*). In Uzbekistan 531 dogs were investigated using arecoline purgation. Of these 279 were farm dogs of which 56 were shown to be infected (20.1%). Of the remaining 240 village dogs, 19 were infected (7.9%). The differences between the prevalence of the two populations is significant ($p<0.001$, Fisher test) (Aminjanov and Aminjanov, *2004*). In Kazakhstan there were similar differences between farm dogs and village dogs. A study in southern Kazakhstan indicated that farm dogs had a prevalence of 23% and an abundance of 631 parasites per dog, whilst village dogs had a much lower prevalence of just 5.8% with an abundance of 27 parasites per dog (Torgerson *et al. 2003c*). The differences in prevalence between these groups of dogs was hypothesized to be due to availability of sources of offal. Farm dogs are used largely for shepherding and presumably have greater access to casualty animals. Village dogs, in contrast tend to be kept more as domestic pets. A separate study in Jalanash in eastern Kazakhstan revealed a prevalence of 13% in a population of 632 dogs with a mean abundance of 812 parasites per dog (Torgerson *et al. 2009a*). In Kyrgyzstan in Naryn province approximately 19% of dogs are infected with *E. granulosus* (Ziadinov *et al. 2008*). Limited information is available on genotypes of *E. granulosus* and all information is from samples recovered from dogs. Genotypes G1 (*E. granulosus* senso stricto), G4 (*E. equinus*) and G6/7 (*E. canadensis*) have been recovered from dogs in either Kazakhstan and/or Kyrgyzstan (Stefanić *et al. 2004*; Ziadinov *et al. 2008*)

In Kazakhstan a small study of 41 wolves found 8 infected with *E. granulosus* (19.5%) (Abdybekova and Torgerson, *2012*). No information is available if the wolves are infected through a wild life cycle or infected through scavenging on sheep.

EPIDEMIOLOGY OF *ECHINOCOCCUS MULTILOCULARIS*

Human studies

Human alveolar echinococcosis (AE) has been diagnosed in central Asia in both Kazakhstan and Kyrgyzstan for many years. The first report in Kyrgyzstan was in 1948 from archival material dating from as early as 1935. Further cases were reported in the Soviet Literature between 1960 and 1988 (reviewed by (Abdyjaparov and Kuutubaev, *2004*). In Kazakhstan, 19 of 1435 cases of echinococcosis reported in Almaty hospitals between 1989 and 2003 were possible AE cases, whilst

4 cases of 205 cases of echinococcosis treated at the Institute of Experimental Surgery in Almaty were confirmed as AE (Shaikenov and Torgerson, *2004*).

Recently strong evidence that human AE is an emergent diseases has been reported, at least in Kyrgyzstan. Up until 2003, only sporadic cases were reported, typified by the summaries given above. But since then, from just 0-3 cases per year, the numbers of AE cases now being reported is over 60 cases per year (Usubalieva *et al. 2013*) (Figure 1). The cases have all been confirmed histologically and the evidence appears to appoint to a newly emerging epidemic rather than improved diagnosis. Naryn district has by far the highest incidence with over 7 cases per 100,000 per year for 2010-2011. However, cases are being seen in every district of Kyrgyzstan. Approximately 64% cases are in females and the mean age of diagnosis is much younger than in Europe at just 33.4 years of age compared to 54 years in Switzerland for example. It is likely that the relative youth of cases of human AE is a reflection of the population structure of the country as the median age of the Kyrgyz population is just 24 years.

Although it is likely that *E. multilocularis* is endemic in the other three republics of central Asia, at the time of writing it was not possible able to access any data or reports other than those described for Kazakhstan and Kyrgyzstan.

Intermediate hosts

This parasite has long been known to be endemic in central Asia with extensive studies being undertaken by Shaikenov in intermediate hosts both before and after the dissolution of the Soviet Union. Much of the data from these studies is reviewed in Shaikenov (*2004a, 2004b, 2006*). From data collected over several decades it was shown that *E. multilocularis* has a very patchy distribution in Kazakhstan. In arid regions infection of small mammals are usually only found in areas where there is moisture or higher levels of humidity such as in desert oases or river and stream valleys. In the mountains in the south of Kazakhstan or the forest steppe in the north, infections of small mammal hosts appear to be more extensive. In Kyrgyzstan there have been studies on rodents of mountainous pastures (Abdyjaparov and Kuttubaev, *2004*). Prevalences of up to 4% were seen in species such as the grey marmot (*Marmota baibacina)* and Gopher (*Citellus relictus*), with a number of other species also being infected.

Definitive hosts

A recent study of red foxes (*Vulpes vulpes*) in Naryn region indicated a high prevalence of approximately 65% (Ziadinov *et al. 2010*). Infection of domestic dogs has been recorded in the mountainous region of south east Kazakhstan. This was first detected in a study in 2002. Of 131 dogs 6 were shown to be infected with *E. multilocularis* (Stefanić *et al. 2004*). One of these dogs was infected with both *E. granulosus* and *E. multilocularis*. This is one of the first reports of a naturally occurring dual infection with both parasites in a dog. Subsequent studies in the same district between 2003 and 2005 indicated a prevalence of 5% (29 of 632 dogs) using arecoline purgation (Torgerson *et al. 2009a*). However because of the poor sensitivity of arecoline purgation the true prevalence is likely to be higher. In Naryn province, Kyrgyzstan, a prevalence of 18% was estimated in dogs using a combination of arecoline purgation and PCR methods and estimating the true prevalence using latent class methods (Ziadinov *et al. 2008*) (Table 2). Dogs that were not tied and hence had greater opportunities to roam, hunt and scavenge had substantial higher prevalences (26%) than dogs that were tied up for most of the time (11%).

Hypothesis for human AE emergence in Kyrgyzstan

The emergence of AE in Kyrgyzstan could be linked to the socio-economic changes that occurred following the dissolution of the Soviet Union. There was certainly increased transmission of CE to humans as outlined above. Thus it can be hypothesised that with increased numbers of dogs and widespread rural poverty *E. multilocularis* colonised dogs which were forced to hunt or forage for food, as suggested by the higher relative risk of infection in free roaming dogs (Ziadinov *et al. 2008*). So it is possible that following colonisation of dogs, the increase in AE is a result of increased dog-human contact. Such increased dog-human contact is proven by the increasing incidence of human CE since dogs are the obligatory definitive host of *E. granulosus*. In addition the increase in the numbers of AE cases appeared approximately 15 years after the dissolution of the Soviet Union, which is the same as the estimated latent period of AE in humans. Further investigations are being undertaken and unpublished evidence suggests that in some communities the ultrasound prevalence of AE may be as high as 7%.

CONCLUSIONS

It is clear that there has been a substantive increase in the numbers of cases of human echinococcosis being diagnosed since the collapse of the Soviet Union. Likewise there appears to be increases in the prevalences of *E. granulosus* in livestock and in dogs. Both these phenomena are likely caused by the reorganisation of livestock farming with the privatisation of large collectivised livestock units. This also led to the closure of large meat processing units and less supervision of meat processing by the veterinary public health services. Dog populations increased and there was a requirement of larger numbers of dogs for shepherding the increased numbers of small livestock units. This provided the opportunity for increased transmission of *E. granulosus* (Shaikenov *et al.* 2003). Increases in free roaming dog populations scavenging for food may have provided an opportunity for *E. multilocularis* to colonise dogs and the close contact of dogs with humans has allowed transmission of *E. multilocularis* from dogs to humans. These may be the reasons that there are now increasing numbers of human AE cases being reported in Kyrgyzstan (Usubalieva *et al. 2013*).

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LEGEND FOR FIGURE

Figure 1. Changes in the numbers of reported cases of human AE in Kyrgyzstan, 1996-2011 (data from Usubalieva *et al. 2013*).

Table 1. Changes in the annual reported incidence of echinococcosis in central Asia following the collapse of the Soviet Union

	Changes in Annual Incidence (year)		Source
Kazakhstan	1.4 per 100,000 (1991)	6.5 per 100,000 (2003)	(Shaikenov and Torgerson, 2004; Torgerson *et al.* 2002)
Kyrgyzstan	5 per 100,000 (1991)	20 per 100,000 (2002)	(Kuttubaev *et al.* 2004; Torgerson *et al.* 2003b)
Tadjikistan	6.8 per 100,000 (1992)	28 per 100,000 (2002)	(Muminov *et al.* 2004)
Turkmenistan	c 6 per 100,000 (1978)	17 per 100,000 (2000)	(Torgerson *et al.* 2006)
Uzbekistan	2 per 100,000 (1988, official figures)	c 5 per 100,000 (2000-2001, official figure) c 17 per 100,000 (case finding studies 2000-2001)	(Aminjanov and Aminjanov, 2004; Nazirov *et al.* 2002)

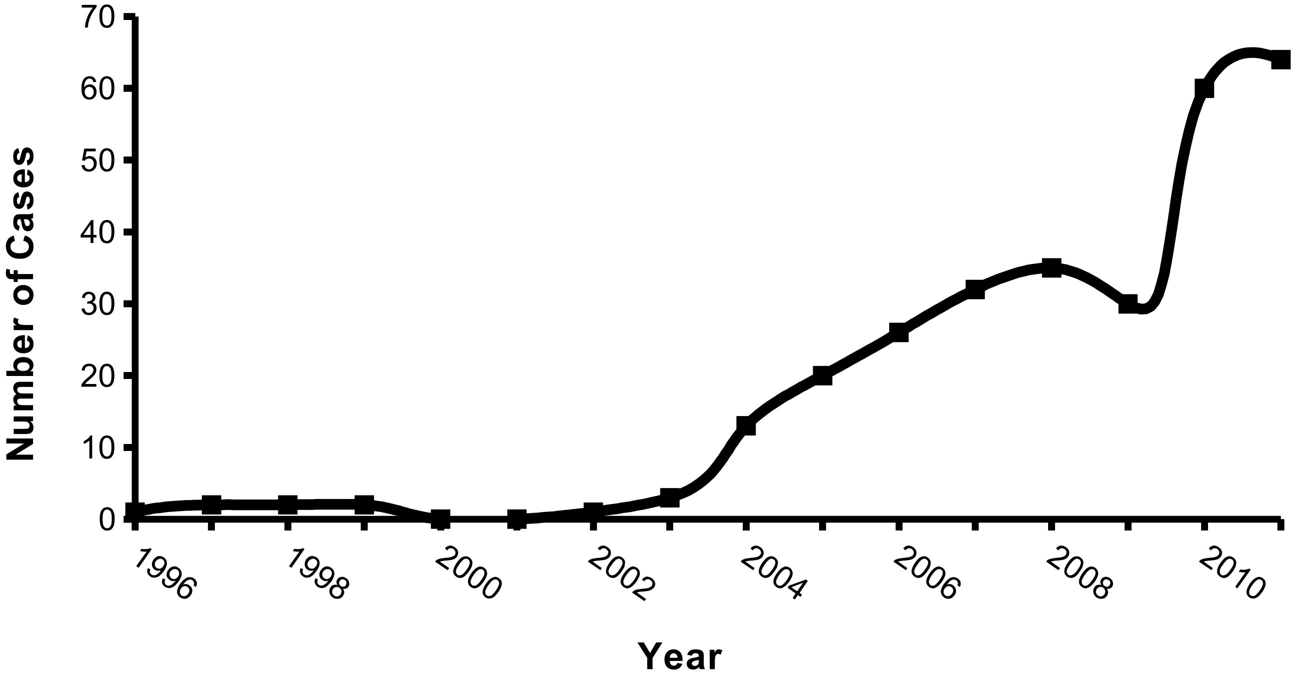
Table 2. Summary of livestock prevalences and transmission dynamics reported from central Asia

Region	Date of study	Host species	Findings	Reference
South Kazakhstan	2001-2002	Sheep	732 (34%) of 2,152 infected. Infection pressure 23% per year	(Torgerson *et al.* 2003a)
Kazakhstan	2001-2002	Sheep	169 (48%) of 353 infected. Infection pressure 29% per year.	(Torgerson *et al.* 2003a)
South Kazakhstan	2001-2002	Cattle	31 (7.2%) of 431 infected. Infection pressure 2.7% per year	(Torgerson *et al.* 2003a)
Naryn, Kyrgyzstan	2006	Sheep	694 (64%) of 1,081 infected	(Torgerson *et al.* 2009b)
Central Tajikistan	Not stated	Sheep and goats	401 (11.8%) of 3400 infected	(Muminov *et al.* 2004)
Southern Tajikistan	Not stated	Sheep and goats	*36.2% in adults, 7.8% in young animals, 25.2% in goats	(Muminov *et al.* 2004)
Central Tajikistan	Not stated	Cattle	*2.5%	(Muminov *et al.* 2004)
South-west and east Tajikistan	Not stated	Cattle	*7.9%	(Muminov *et al.* 2004)
Tajikistan	Not stated	Pigs	33 (2.1%) of 1,601 animals	(Muminov *et al.* 2004)
Uzbekistan	1990-2002	Sheep	*Increasing from 45% to 62%	(Aminjanov and Aminjanov, 2004)
Uzbekistan	1990-2002	Goats	*Increasing from 8% to 11.1%	(Aminjanov and Aminjanov, 2004)
Uzbekistan	1990-2002	Cattle	*Increasing from 24% to 46%	(Aminjanov and Aminjanov, 2004)
Uzbekistan	1990-2002	Camels	*Increasing from 25% to 35%	(Aminjanov and Aminjanov, 2004)

*Sample sizes not stated in original references

Table3. *Echinococcus* in definitive hosts in central Asia

Region	Date of study	Host species	Diagnostic method	Findings	Reference
Villages, south Kazakhstan	1999-2001	Dog	Arecoline purgation	90 (5.8%) of 1,552 infected with *E. granulosus*. Mean abundance 27 parasites per dog	(Torgerson *et al.* 2003c)
Farms, South Kazakhstan	1999-2001	Dog	Arecoline purgation	145 (23%) if 630 farms dogs infected with *E. granulosus*. Mean abundance 631 parasites per dog	(Torgerson *et al.* 2003c)
Jalanash, south east Kazakhstan	2002	Dog	PCR and arecoline purgation	8 of 131 (26%) dogs infected with *E. granulosus,* 6 of 131 (4.6%) infected with *E. multilocularis.* One dog was infected with both parasites	(Stefanić *et al.* 2004)
Jalanash, South east Kazakhstan	2003-2005	Dog	Arecoline Purgation	85 (13%) of 632 dogs infected with *E. granulosus*. Mean abundance 812 parasites. 29 (5%) of 632 dogs infected with *E. multilocularis*. Mean abundance 72 parasites per dog	(Torgerson *et al.* 2009a)
South Kazakhstan	2001-2008	Wolf	Necropsy	8 of 41 (20%) wolves infected with *E. granulosus*. Mean abundance of 1275 parasites per wolf	(Abdybekova and Torgerson, 2012)
Naryn District, Kyrgyzstan	2005	Dog	Arecoline purgation, PCR of faeces	True prevalence in dogs of *E. granulosus* 19% and *E multilocularis* 18% in 466 dogs	(Ziadinov *et al.* 2008)
Kyrgyzstan	1991-2001	Dog	Necropsy	Increase in prevalence from 4.8% to 11.2% of *E. granulosus*	(Kuttubaev *et al.* 2004)
Naryn District, Kyrgyzstan	2006-2007	Fox	Necropsy	96 (64%) of 151 foxes infected with *E. multilocularis.* Mean abundance of 8,669 parasites per fox.	(Ziadinov *et al.* 2010)
Tajikistan	Not stated	Dog	Necropsy	18 (15%) of 120 dogs infected with *E. granulosus*	(Muminov *et al.* 2004)
Uzbekistan	c 2003	Dog	Arecoline purgation	56 (20%) of 279 farm dogs infected with *E. granulosus*	(Aminjanov and Aminjanov, 2004)
Uzbekistan	C 2002	Dog	Arecoline purgation	19 (7.9%) of 240 village dogs infected with *E. granulosus*	(Aminjanov and Aminjanov, 2004)


Number of Cases
0
10
20
30
40
50
60
70
1996
1998
2000
2002
2004
2006
2008
2010
Year